APPENDIX

ROBUST SUMMARIES

U.S. HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

ROBUST SUMMARY

Phosphorous acid, triisodecyl ester (CAS# 25448-25-3)

Prepared by:

General Electric Company
on behalf of the
Phosphite Producers HPV Consortium

and

Phosphite Manufacturers Consortium

Washington, D.C., USA

September 10, 2001

Prepared for:

U.S. Environmental Protection Agency

Washington, D.C., USA

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PHOSPHOROUS ACID, TRIISODECYL ESTER (CAS # 25448-25-3)

PHYSICAL AND CHEMICAL DATA

1.0 MELTING POINT

No studies were found.

2.0 BOILING POINT

No studies were found.

3.0 VAPOR PRESSURE

No studies were found.

4.0 PARTITION COEFFICIENT ($log_{10}P_{ow}$)

No studies were found.

5.0 WATER SOLUBILITY

5.1. Solubility

No studies were found.

5.2. pH Value, pKa Value

No studies were found.

ENVIRONMENTAL FATE AND PATHWAYS

6.0 PHOTODEGRADATION

No studies were found.

7.0 STABILITY IN WATER

No studies were found.

8.0 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS, INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

8.1. TRANSPORT

No studies were found.

8.2. THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

No studies were found.

9.0 BIODEGRADATION

No studies were found.

ECOTOXICOLOGICAL DATA

10.0 ACUTE/PROLONGED TOXICITY TO FISH

No studies were found.

11.0 TOXICITY TO AQUATIC PLANTS (e.g., Algae)

No studies were found.

12.0 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

No studies were found.

TOXICITY

13.0 ACUTE TOXICITY

13.1 ACUTE ORAL TOXICITY

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rats/Sherman-Wistar
Sex:	Males and females
# Animals:	5/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).

Value:	> 5 g/kg
Method:	Other (1981). The method employed in the testing, evaluation, and the scoring of the results was adopted from the U.S. Federal Hazardous Substances Act Regulations study guidelines, 16 CFR, section 1500.3. [Comparable to OECD Test Guideline 401] *Description of test procedure*: Albino rats weighing between 200 and 300 grams were dosed in an initial limit test via oral gavage with 5 g/kg body weight. Animals were fasted overnight, but were not deprived of water. Following administration the animals were allowed food and water *ad libitum* for a 21-day observation period, during which time the rats were observed daily for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3. The LD50 was calculated using the method described by Finney, D.J. 1971. 'Statistical Methods in Biological Assay, 2nd Edition, London Griffen Press.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Triisodecyl phosphite (CAS# 25448-25-3, Lot #TDPx-003-04070A from Borg Warner Company, Parkersburg, WV) Commercial, purity: $\geq$ 97% (Phosphorus content = 6.17 %)
Remarks:	After 1-2 hours, the animals appeared depressed and ruffled. After 24 hours they appeared improved and within 48 hours they were essentially normal, with the exception of one male that died on day 2. Gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions.

13.2 ACUTE INHALATION TOXICITY

Type:	LC_0 [ ]; LC_{100} [ ]; LC_{50} [X]; LCL_0 [ ]; Other [ ]
Species/strain:	Rats/Sherman-Wistar
Sex:	Males and females
# Animals:	5/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Exposure time:	One hour
Value:	> 12.6 mg/L (maximum attainable concentration)
Method:	Other (1980). [Comparable to OECD Test Guideline 403] *Description of test procedure*: The animals were exposed to the test material inside a 260-L Plexiglas exposure chamber for one hour. The material was administered as an aerosol, which was generated by a six-jet Collision nebulizer (BGI Incorporated, Waltham, MA). The air was passed through a desiccant prior to being passed through the test material. The rate of flow through the chamber was 20 L/min at a temperature of 72° F. The average concentration of the aerosol over the one-hour exposure period was calculated to be 12.6 mg/L by differential weighing of the flask from which the aerosol was generated. The particle size

(mass median diameter) of the aerosol of the test material was determined, to assure that the animals received a respirable dose, using an Andersen Sampler cascade impactor. The sampler was run for 5 minutes midway through the exposure. During sampling, air from the breathing zone of the animals was drawn through the cascade impactor at the rate of 1 ft^3/min. The amount of aerosol impacting on each plate of the Andersen Sampler was determined by differential weighing. From these values the mass median diameter of the aerosol was calculated to be 0.48 microns and the concentration was calculated to be 0.10 mg/L. Following one hour of inhalation exposure, the animals were returned to their cages and observed daily for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.

GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Triisodecyl phosphite (CAS# 25448-25-3, Lot #TDPx-003-04070A from Borg Warner Company, Parkersburg, WV) Commercial, purity: $\geq$ 97% (Phosphorus content = 6.17 %)
Remarks:	No adverse effects were observed during the one-hour exposure period. No untoward signs and symptoms were observed during the 21-day post-exposure observation period. No animals died during the experiment and gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions.

13.3 ACUTE DERMAL TOXICITY

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rabbits/New Zealand White
Sex:	Males and females
# Animals:	3/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Value:	> 5 g/kg
Method:	Other (1980). The method employed in the testing, evaluation, and the scoring of the results was similar to the methods described in Section 1500.40 of the U.S. Federal Hazardous Substances Act Regulations, 16 CFF, pg. 123. [Comparable to OECD Test Guideline 402] *Description of test procedure*: Albino rabbits weighing between 2.0 and 3.0 kg each were used in this study. All animals had their backs clipped free of hair 24 hours prior to testing and had their backs abraded prior to dosing. The sample was applied as supplied to the back of each animal at a dose of 5.0 g/kg body weight. These treated areas were covered with large gauze patches and an impervious material was wrapped around the trunk of each animal. The dressings were removed after 24 hours and any excess material was removed. The animals were observed for a 21-day

period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triisodecyl phosphite (CAS# 25448-25-3, Lot #TDPx-003-04070A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: $\geq$ 97% (Phosphorus content = 6.17 %)

Remarks: No animals died during the experiment and there were no signs of toxicity, except for substantial skin irritation lasting over several days. Gross pathological examination revealed no remarkable findings.

Reference: Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA

Reliability: (Klimisch Code 1) Valid without restrictions. Comparable to OECD 402, except this limit test used 3 animals/sex rather than 5/sex as recommended by the OECD guideline.

14.0 GENETIC TOXICITY *IN VITRO* OR *IN VIVO* (CHROMOSOMAL ABERRATIONS)

Type: Micronucleus test

Species/strain: Mouse/CD-1

Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]

# of Animals: 5/sex

Route of Administration: Oral, gavage

Exposure period: Two single doses administered over 24 hours

Doses: 0, 4450, 9100, and 18200 mg/kg (total dose)

Results: *Effect on mitotic index or PCE/NCE ratio*: There was no statistically significantly difference between any of the test article treatments and the negative control.
Genotoxic effects: Negative

Method (Year): Other (1981). The protocol used is comparable to OECD Test Guideline 474

Description of test procedure: All animals weighted between 18 and 21 grams and were group-housed in plastic caging maintained in a controlled environment (temperature 22^{o}C, 30 air changes/hour, 12-hour light/dark cycle, and access to food and water *ad libitum*). The animals were fasted overnight prior to dosing. A preliminary range-finding toxicity study was performed prior to the conduct of the definitive assay to determine the maximum tolerated dose (MTD) of the test article. The MTD was designed to produce one or two deaths over the treatment period. From the results of the preliminary test, doses of 0, 4450, 9100, and 18200 mg/kg were used in the main study. The test article was administered (diluted in corn oil) via oral gavage to groups of mice (5/sex), at a volume of 0.1 mL per 10 grams of body weight. The concurrent positive control group was given an intraperitoneal injection of mitomycin C at a concentration of 0.4 mg/mL. Following the last dose, the animals were observed for six hours, sacrificed, and both femurs were removed from each animal. A direct bone marrow smear from each femur was placed

onto a slide and prepared for microscopic analysis to determine the incidence of micronucleated cells per 1000 polychromatic erythrocytes per animal and the ratio of normochromatic to polychromatic erythrocytes (PCE/NCE ratio).

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triisodecyl phosphite (CAS# 25448-25-3, Lot #TDPx-003-04070A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: ≥ 97% (Phosphorus content = 6.17 %)

Remarks: After administration of TDP at 9100 and 18200 mg/kg, signs of toxicity (piloerection and lethargy) were observed 30 minutes after dosing in all animals. The symptoms decreased over the next several hours and were not observed 6 hours after administration. No toxic reactions were observed in the corn oil negative control group or the 4450 mg/kg TDP group. After administration of mitomycin C, no toxic reactions or mortality were observed.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal and the PCE/NCE ratios for all test groups and both controls are presented below:

Test Group	# Micronucleated Cells per 1000 PCEs/animal mean (range)	PCE/NCE Ratio mean (range)
Negative Control	1.9 (0–4)	1.75 (1.15–3.93)
4450 mg/kg TDP	1.2 (0–3)	2.21 (1.05–4.22)
9100 mg/kg TDP	1.0 (0–2)	1.61 (0.76-2.44)
18200 mg/kg TDP	2.7 (0–5)	2.34 (1.62–3.55) *
Mitomycin C	89.1 (13-182)	8.61 (2.25-16.67)
*Historical Control***	*0.79 (0.1-1.8)*	*0 - 5*

* For all three TDP groups in both sexes, the micronucleus counts were not statistically different from the concurrent control values. For the PCE/NCE ratio, the 18200 mg/kg TDP group was statistically different from the concurrent control value ($p < 0.01$).

The positive control group, mitomycin C, produced statistically significant increases in both the number of micronucleated cells per 1000 PCEs/animal and the PCE/NCE ratio.

** The historical control values from this laboratory were based on the previous 18 experiments. In this experiment, the negative control mean value of 1.9 (range = 0-4) for the number of micronucleated cells per 1000 PCEs per animals was higher than the historical control value.

Based on the conditions of this study, it was concluded that the test article, TDP, failed to show any evidence of mutagenic potential when administered orally to either sex. Evidence of toxicity to bone marrow was evident only at the highest total dosage of 18200 mg/kg body weight in both males and females.

Criteria for evaluating results: A material was considered to show evidence of mutagenic activity if it produced a statistically significant increase in micronucleated cells compared to the concurrent negative control group values. Due to heterogeneity of variance [Bartlett's test; $p<0.01$], non-parametric methods based on Kruskal-Wallis mean ranks were used to analyse the micronucleated cell counts. If the erythrocyte ratios at the top dose were significantly different from the concurrent negative control values, then the ratios of the two lower doses were scored.

Reference: Richold et al. (1981). Unpublished report TCO 17E/81311 entitled "Micronucleus test on triisodecyl phosphite (TDP)", dated June 25, 1981 for Tenneco Chemicals Inc., Saddle Brook, NJ from Huntingdon Research Centre, Cambridgeshire, England

Reliability: (Klimisch Code 1) Valid without restrictions.

15.0 GENETIC TOXICITY *IN VITRO*

15.1 BACTERIAL TEST

15.1.1

Type: Bacterial reverse mutation assay (Ames test)

System of testing: *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA 1538

Concentration: 0, 10, 100, 500, 1000, 5000 µg/plate

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 5000 µg/plate
Without metabolic activation: > 5000 µg/plate

Precipitation conc.: 1000 and 5000 µg/plate

Genotoxic effects:

	+	?	-
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

Method (Year): Based on Ames et al. (1975) *Mut. Res*., 31:347. The protocol is comparable to OECD Test Guideline 471

Description of test procedure: The test substance was dissolved in ethanol at 50 mg/mL and lower concentrations (0.5 - 10 mg/mL) were prepared by subsequent serial dilution with ethanol. One-tenth mL aliquots of these solutions were used to assay the test substance at 10 – 5000 µg/plate. Concurrent positive controls requiring metabolic activation (TA-1535, cyclophosphamide at 200 µg/plate; TA-1537, TA-1538, TA-98, and TA-100, benzo[a]pyrene at 5 µg/plate) and positive controls not requiring metabolic activation (TA-1535 and TA-100, 1 µg/plate sodium azide; TA-1537, 50 µg/plate 9-aminoacridine; TA-1538 and TA-98, 10 µg/plate 2-nitrofluorene) were run for each strain. All controls and test plates were incubated at 37°C for 48 –hours, examined for the appearance of a normal background lawn, and macroscopic colonies were enumerated.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triisodecyl phosphite (CAS# 25448-25-3, Lot #TDPx-003-04070A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: $\geq$ 97% (Phosphorus content = 6.17 %)

Remarks: The number of revertants produced by treatment of the bacteria with the test at all concentrations and in all tester strains was less than or approximately equal to the number of revertants in the vehicle-treated negative control groups, with and without metabolic activation. The mutagenic indices ranged from 0.8 to 1.4 without S-9 mix and from 0.7 to 1.3 with S-9 mix in all TDP test groups. The positive control groups were

all mutagenic in their appropriate tester strains (mitotic index ranged from 4.0 to 6.9 with metabolic activation and from 10.2 to 70.6 without metabolic activation), indicating that the metabolic activation system was working properly and all strains were capable of mutation. The test material TDP was therefore concluded to not be mutagenic in this assay.
Criteria for evaluating results: The assay was scored as the ratio of the number of macroscopic colonies on the test plate over the number of macroscopic colonies on the control plate (mutagenic index). The test compound was considered to have a positive response if the mutagenic index was greater than 2.0 and the mutagenicity exhibited a dose-response relationship.
Plates/test: Samples were run in duplicate, with and without metabolic activation.
Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.
Media: Aqueous agar solution

Reference: Van Goethem, D. 1980. Unpublished report no 4822-E entitled "Evaluation of triisodecyl phosphite in the *Salmonella*/microsome (Ames) assay" dated September 30, 1980, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.1.2

Type: DNA repair-suspension assay

System of testing: *Escherichia coli* tester strains W3110 (pol A^+) and p3478 (pol A^-)

Concentration: 0, 0.1, 1, 5, 10, and 50 µg/mL

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 50 µg/mL
Without metabolic activation: > 50 µg/mL

Precipitation conc.: 50 µg/mL

Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative

Method (Year): Based on Slater et al. (1971) *Cancer Res*. 31:970-973.
Description of test procedure: The test substance was dissolved in ethanol at 5 mg/L. All doses were prepared by subsequent serial dilution with ethanol. Aliquots (0.1 mL) of these solutions were used to assay the test material at concentrations of 0.1 to 50 µg/mL of bacterial suspension. Plates were incubated for 18 hours at 37° C and the number of viable cells was recorded. The concurrent positive control for the metabolic activation group was 2-aminofluorene (200 µg/mL) and N-methyl-N'-nitrosoguanidine (2 µg/mL) served as the positive control for the group without metabolic activation.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triisodecyl phosphite (CAS# 25448-25-3, Lot #TDPx-003-04070A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: ≥ 97% (Phosphorus content = 6.17 %)

Remarks: The survival indices at all doses for the test material were greater than 0.80, with or without metabolic activation (0.86 to 1.01 without metabolic activation; 1.04 to 1.28 with metabolic activation). The survival indices for the positive controls were 0.64 and 0.41 for the groups with and without metabolic activation, respectively. The test material TDP was therefore concluded to not cause preferential killing of the repair-deficient strain in this assay.

Criteria for evaluating results: The suspension test is scored as the ratio of the number of pol A^- survivors over the number of pol A^+ survivors (Survival Index). A test material is considered positive if the Survival Index is less than 0.8 and the differential toxicity exhibits a dose-response relationship.

Plates/test: Samples were run in duplicate, with and without metabolic activation.

Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.

Media: Aqueous agar solution

Reference: Van Goethem, D. 1981. Unpublished report no. 4822-E entitled "Evaluation of triisodecyl phosphite in the E. coli DNA repair suspension assay" dated January 19, 1981, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.2 NON-BACTERIAL *IN VITRO* TEST (MAMMALIAN CELLS)

No studies were found.

16.0 REPEATED DOSE TOXICITY

No studies were found.

17.0 REPRODUCTIVE TOXICITY

No studies were found.

18.0 DEVELOPMENTAL TOXICITY/TERATOGENICITY

No studies were found.

U.S. HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

ROBUST SUMMARY

Phosphorous acid, diisodecyl phenyl ester (CAS# 25550-98-5)

Prepared by:

General Electric Company
on behalf of the
Phosphite Producers HPV Consortium

and

Phosphite Manufacturers Consortium

Washington, D.C., USA

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PHOSPHOROUS ACID, DIISODECYL PHENYL ESTER (CAS# 25550-98-5)

PHYSICAL AND CHEMICAL DATA

1.0 MELTING POINT

No studies were found.

2.0 BOILING POINT

No studies were found.

3.0 VAPOR PRESSURE

No studies were found.

4.0 PARTITION COEFFICIENT ($log_{10}P_{ow}$)

No studies were found.

5.0 WATER SOLUBILITY

5.1. Solubility

No studies were found.

5.2. pH Value, pKa Value

No studies were found.

ENVIRONMENTAL FATE AND PATHWAYS

6.0 PHOTODEGRADATION

No studies were found.

7.0 STABILITY IN WATER

No studies were found.

8.0 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS, INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

8.1 TRANSPORT

No studies were found.

8.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

No studies were found.

9.0 BIODEGRADATION

Type: aerobic [X]; anaerobic [ ]
Inoculum: adapted [X]; non-adapted [ ];
Concentration of the chemical: 10.9 mg/L and 20.7 mg/L
related to COD [X]; DOC [ ]; Test substance [ ];
Medium: water [ ]; water-sediment [ ]; soil [ ];
sewage treatment [X]
Contact time: 28 Days
Degradation: 10% in 28 days (test concentration; 10.9 mg/L)
4% in 28 days (test concentration; 20.7 mg/L)
Results: Readily biodeg. [ ]; Inherently biodeg. [ ]; under test condition no biodegradation observed [X], Other [ ]
Kinetic of test substance: Test substance not readily biodegradable. Kinetics (% degradation of test substance against time) not provided in the test report
Control substance: Aniline (Merck No. 1261) (20 mg/L)
Kinetic of control substance: 88% in 28 days. Kinetics (% degradation of test substance against time) not provided in the test report
Degradation Products: Yes [ ] No [ ] Not measured [X]
Method (Year): 84/449/EEC C.5, Biotic degradation: modified Sturm test [Comparable to OECD 301B]

Description of test procedure: The test system/inoculum (bacteria) was collected from activated sludge of a sewage treatment plant (CH-4153 Reinach) and had a pH of 7.6. The test vessels (2-L flasks with dark brown glass) were equipped with gas inlet and magnetic stirrer. Mineral solution (1200 mL) with the inoculum was aerated for 24 hours in each test vessel. The test substance (31 mg) was mixed with 15 mL of Tween 80 (polyoxyethylene-sorbitan-monooleate), homogenized, and added to the test vessel, which was immediately connected to the CO_2 traps. The blank control was a mixture of Tween 80 and water, the reference substance was aniline, and both were run in duplicate. All test media were controlled to 22 +/- 2^oC and the supplied air (25 mL/min) was free from carbon dioxide. The concentration of test substance was 10.9 mg/L and 20.7 mg/L and the theoretical carbon dioxide ($ThCO_2$) evolution was 47.32 and 89.99 mg CO_2/1.5 L, respectively. The calculation of $ThCO_2$ was based on the chemical formula of the test substance, C30H63P. Measurements included the determination of the initial CO_2 of 0.05 N sodium hydroxide

and the CO_2 absorbed in the absorbers filled with 200 mL of 0.05 N sodium hydroxide on days 0, 3, 6, 9, 13, 16, 20, 23, 27, and 28. The biodegradation was calculated on the basis of the theoretical carbon content of the test substance and the cumulative quantities of CO_2 determined on the days of measurements.

GLP: Yes [X] No [ ] ? [ ]

Test Substance: Irgastab CH 300 (CAS# 25550-98-5)
Commercial, purity: Stated to be 'within specifications'; Commercial batch no. 09520538 (Test identification code: TK 11211) from Ciba-Geigy, Ltd, Basel, Switzerland

Remarks: The test substance was determined to be 'not readily biodegradable' in this test. The measured CO2 evolution and biodegradation (%) were as follows:

CO2 Evolution (mg)

	Controls		Test Substance	
Day	Blank	Aniline	10.9 mg/L	20.7 mg/L
3	3.4	3.3	3.6	3.4
6	4.8	42.5	5.5	5.3
9	6.3	62.7	7.3	6.9
13	7.7	72.0	9.0	8.6
16	8.1	76.8	10.2	10.2
20	9.3	80.2	12.4	11.6
23	10.1	81.5	12.9	12.2
27	21.4	91.7	26.2	27.1
28	11.5	88.9	16.4	14.8

Biodegradation (%)

	Control		Test Substance	
Day	Blank	Aniline	10.9 mg/L	20.7 mg/L
3	-	0	0	0
6	-	50	1	1
9	-	68	2	1
13	-	75	3	1
16	-	80	4	2
20	-	82	7	3
23	-	82	6	2
27	-	84	10	6
28	-	88	10	4

Reference: Grade, R. 1993. Unpublished report no. 928303 entitled "Report on the test for ready biodegradability in the modified sturm test of Irgastab CH 300", dated December 11, 1992 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: Acceptable and well-documented study report that meets basic scientific principles.

ECOTOXICOLOGICAL DATA

10.0 ACUTE/PROLONGED TOXICITY TO FISH

Type of Test:	Static [X] Semi-static [ ] Flow-through [ ] Other [ ] Open-system [ ] Closed-system [ ]
Species/Source:	Golden Orfe (*Leuciscus idus*)
Exposure Period:	48 Hours
Results:	LC_{50} (48h) = > 100 mg/L LC_{50} (24h) = > 100 mg/L NOEC = > 100 mg/L LOEC = > 100 mg/L
Analytical Monitoring:	Yes [X] No [X] ? [ ]
Method (Year):	84/449/EEC C.1 Acute toxicity for fish [Comparable to OECD 203] *Description of test procedure*: The highest concentration of test substance in water was determined to be 100 mg/L, based on visible precipitate immediately forming at concentrations above this value. The test substance was prepared by dissolving 5.0 g into 50 mL of DMSO. No analytical calculations of test concentrations were performed, but the material appeared to be homogeneously distributed. The acute toxicity in fish was determined using the limit test at a single nominal concentration of 100 mg/L of test substance. Duplicate test article groups were used and compared to that of concurrent blank (water) and vehicle control (1101 mg DMSO/L water) groups. Ten fish (supplied by P. Hohler, Zeiningen, Switzerland) per group per tank were used. The mean fish length was 44 mm (35-50 mm) and the mean weight was 0.59 g (0.29-0.85g). The loading of fish in the tank was 0.39 g fish/L water. Fish were acclimatised for 22 days prior to the experiment and not fed for 3 days prior to or during exposure. Each 20-L tank was filled with 15 L of dechlorinated tap water (carbon filter). The water hardness was 254 mg CaCO3/L, the index of condition (K) was 0.7 g/cm3, and the temperature was maintained at 21 +/- 1^{o}C. Gentle aeration during the test and fluorescent light, 16-hours daily were used. Calculated amounts of the test substance to produce the desired test concentrations were added into the water and were homogeneously distributed. The fish were transferred into the tank for a total duration of 48 hours. Signs and symptoms of toxicity and mortality were recorded at 24 and 48 hours.
GLP:	Yes [X] No [ ] ? [ ]
Test Substance:	Irgastab CH 300 (CAS# 25550-98-5) Commercial, purity: Not stated; Commercial batch no. 928 (Test article identification code: TK 11211) from Ciba-Geigy, Ltd, Basel, Switzerland
Remarks:	No fish died during the experiment. There were no effects on swimming behavior, loss of equilibrium, respiratory function, exophthalmia, or pigmentation in any group. The oxygen content ranged from 97-98 % at 0 hours, 84-94% at 24 hours, and 93-99% at 48 hours. The pH ranged from 7.8 to 8.1 and the water temperature was 20-22°C throughout the experiment.
Reference:	Rufli, H. 1992. Unpublished report no. 884179 entitled “Report on the test for acute toxicity of TK 11211 to Golden Orfe (*Leuciscus idus*)”, dated June 21, 1988 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: (Klimisch Code 1) Valid without restrictions. Comparable to OECD 203 with the exception of a 3-day fast prior to exposure rather than a fast of 24-hours. The exposure duration was 48-hours, not 96-hours as preferred per the study guideline.

11.0 TOXICITY TO AQUATIC PLANTS (e.g., Algae)

Species: Green algae (*Scenedesmus subspicatus*)
End-point: Biomass [ ]; Growth rate [X]; Other [ ]
Exposure period: 72 Hours
Results: Growth: EC_{50} (72 h) = 45 mg/L (95% CI, 25-67 mg/L)
NOEC = 0.3 mg/L
Analytical monitoring: Yes [X] No [ ] ? [ ]
Method (Year): open-system [ ]; closed-system [X]
87/302/EEC, Algal inhibition test [Comparable to OECD 201]
Description of test procedure: Green algae (obtained from Pflanzenphysiologisches Institut University, Gottingen, Germany) with an initial cell density of 10100 cells/mL were used in this experiment. The test vessels, 100-mL Erlenmeyer flasks stoppered with aluminum caps, were filled with 50 mL of test solution per flask. The water composition was reported to be according to the guideline, the temperature was maintained to 23 +/- 1°C, and continuous illumination of white fluorescent light (approx. 8000 lux) was used. The stock solution was made up of 100.2 mg of test substance mixed into 1000 mL of water. Calculated amounts of the stock solution to produce the desired test concentrations were added to the water and were homogeneously distributed. Nominal target concentrations of 1.23, 3.7, 11, 33, and 100 mg of test substance/L were used and each test concentration was tested in 3 replicates. The blank control (water) was tested in 6 replicates. The algae were transferred into the flasks for a total duration of 72 hours. Samples of each test concentration were drawn immediately before exposure and at the end of the experiment and kept at 18-22 °C until analysed. Cell densities were measured at 24, 48, and 72 hours on a "TOA" cell counter. The EC-50 values were calculated according to the maximum likelihood method, logit model.
GLP: Yes [X] No [ ] ? [ ]
Test Substance: Irgastab CH 300 (CAS# 25550-98-5)
Commercial, purity: Stated to be 'within specifications'; Commercial batch no. 09520538 (Test identification code: TK 11211) from Ciba-Geigy, Ltd, Basel, Switzerland
Remarks: The measured test substance concentrations were determined by HPLC to be <0.01, 1, 3.8, 12.1, 33.7, and 107.8 mg/L at 0 hours and <0.01, 0.3, 2.0, 5.9, 21.4, and 75.6 mg/L at 72 hours for the blank and the target concentrations of 1.23, 3.7, 11, 33, and 100 mg/L, respectively. The EC50 and NOEC values reported above were based on these measured concentrations. The pH values of the water ranged from 7.8-7.9 at 0 hours and 8.5 to 9.0 at 72 hours.

The mean cell densities (cells/mL x 10000) were as follows:

	24 hr	48 hr	72 hr
Blank	6.0	27.1	147.3
0.3 mg/L	5.2	28.3	142.8
2.0 mg/L	5.2	26.3	119.5
5.9 mg/L	5.1	23.7	122.7
21.4 mg/L	4.6	23.5	102.8
75.6 mg/L	2.9	10.5	41.7

The mean inhibition levels for the blank control and the 0.3, 2.0, 5.9, 21.4, and 75.6 mg/L test substance groups were 0.0, 1.8, 15.0 16.0, 26.2, and 69.6%, respectively.

Reference: Grade, R. 1993. Unpublished report no. 928304 entitled "Report on the growth inhibition test of Irgastab CH300 to Green Algae (*Scenedesmus subspicatus*)", dated June 28, 1993 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: (Klimisch Code 1) Valid without restrictions.

12.0 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

12.1 *Daphnia*

Type of test: static [X]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]

Species: *Daphnia magna* (Straus 1820)

Exposure period: 48 hours

Results: EC_{50} (24h) = 0.6 mg/L (95% Confidence Limit; 0.4-1.2 mg/L)
EC_{50} (48h) = 0.2 mg/L (95% Confidence Limit; 0.1-0.4 mg/L)
EC_0 (48h) = < 0.04 mg/L
EC_{100} (48h) = > 0.83 mg/L
NOEC = < 0.04 mg/L
LOEC = 0.04 mg/L

Analytical monitoring: Yes [X] No [ ] ? [ ]

Method: 84/449/EEC C.2, Acute toxicity for *Daphnia* [Comparable to OECD 202]

<u>*Description of test procedure*</u>: Cultures of *Daphnia* (source: Ciba-Giegy ecotoxicology testing facility) were maintained in glass vessels containing approximately 2.5 L of reconstituted water (total hardness: 240 mg/$CaCO_3$/L) at 20 +/- 1^oC and fluorescent lighting was used 16 hours/day. The water was aerated with clean air for at least 24 hours prior to use and was partially renewed three times per week. At each renewal the *Daphnia* were fed with a suspension of green algae (*Scenedesmus subspicatus*) supplemented by a suspension of TETRAMIN-extract. The experimental test vessels consisted of beakers covered with watch glasses and filled with 100 mL of solution. The test substance stock solution was test substance (20.1 mg) mixed with water and made up to 1000 mL. No vehicle was used. Calculated amounts of the stock solution to produce the desired test concentrations were added to the water and were homogeneously distributed. The nominal test concentrations were 0 (blank control), 0.058, 0.1, 0.18, 0.32, 0.58, and

1.0 mg of test substance/L. Analytical determination (limit of detection = <0.01mg/L) of test substance concentration was performed at 0 and 48 hours. One day prior to exposure, Daphnia older than 24 hours of age *Daphnia* were separated from the young by sieving all individuals using an 800 µm sieve. Immediately prior to exposure, this sieving process was repeated and the young (6-24 hours of age) were retained for the test. The *Daphnia* were not fed during the test. There were a total number of 20 *Daphnia* per treatment group and control with 4 replicates of 5 *Daphnia* each. Immobilization was recorded after 24 and 48 hours of exposure. The EC-50 values were calculated according to method described by Berkson (1953; JASA 48:569-599), and the EC-values were graphically determined on gausso-logarithmic probability paper.

GLP: Yes [X] No [ ] ? [ ]

Test Substance: Irgastab CH 300 (CAS# 25550-98-5)
Commercial, purity: Stated to be 'within specifications'; Commercial batch no. 09520538 (Test identification code: TK 11211) from Ciba-Geigy, Ltd, Basel, Switzerland

Remarks: The measured test substance concentrations were determined by HPLC to be <0.01, 0.04, 0.17, 0.38, 0.45, and 0.83 mg/L at 0 hours for the blank and the target concentrations of 0.058, 0.1, 0.18, 0.32, and 0.58, and 1.0 mg/L, respectively. At 72 hours, the measured concentrations were <0.01 for the blank control and lowest three concentrations and 0.14, 0.26, and 0.41 for the target 0.32, 0.58, and 1.0 mg/L groups, respectively. Due to disappearance of test material in the lowest concentrations at 48 hours, the EC50 and NOEC values reported above were based on the measured concentrations at 0 hours rather than at 48 hours. The following are the percent of the immobilized *Daphnia* (n = 20 per test concentration) after 24 and 48 hours for each test group:

	24 Hours	48 Hours
Test Concentration	Total No. (%)	Total No. (%)
Blank	0 (0)	0 (0)
0.04 mg/L	1 (5)	5 (25)
0.17 mg/L	1 (5)	8 (40)
0.38 mg/L	2 (10)	7 (35)
0.45 mg/L	9 (45)	18 (90)
0.83 mg/L	15 (75)	19 (95)

The pH values of the water ranged from 8.0 to 8.6 at 0 hours and 7.8 to 7.9 at 48 hours.

Reference: Grade, R. 1993. Unpublished report no. 928305 entitled "Report on the acute toxicity test of Irgastab CH300 on Daphnia (*Daphnia magna*, Straus 1820)", dated June 10, 1993 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: (Klimisch Code 1) Valid without restrictions.

12.2 Other aquatic organisms

No studies were found.

TOXICITY

13.0 ACUTE TOXICITY

13.1 ACUTE ORAL TOXICITY

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rats/Sherman-Wistar
Sex:	Males and females
# Animals:	5/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Value:	> 5 g/kg
Method:	Other (1981). The method employed in the testing, evaluation, and the scoring of the results was adopted from the U.S. Federal Hazardous Substances Act Regulations study guidelines, 16 CFR, section 1500.3. [Comparable to OECD Test Guideline 401] *Description of test procedure*: Albino rats weighing between 200 and 300 grams were dosed via oral gavage with 5 g/kg body weight. Animals were fasted overnight prior to dosing, but were not deprived of water. Following administration the animals were allowed food and water *ad libitum* for a 21-day observation period, during which time the rats were observed daily for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Diisodecyl phenyl phosphite (CAS# 25550-98-5, Lot #PDDP-002-03240A from Borg Warner Company, Parkersburg, WV) Commercial, purity: Not stated (Phosphorus content = 7.09%)
Remarks:	After 1 hour the animals (number not specified) appeared slightly depressed and ruffled. After 24 hours the animals appeared to improve and within 48 hours the animals were essentially normal. No animals died during the experiment and gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions. Acceptable, well documented study report that meets basic scientific principles.

13.2 ACUTE INHALATION TOXICITY

Type:	LC_0 [ ]; LC_{100} [ ]; LC_{50} [X]; LCL_0 [ ]; Other [ ]
Species/strain:	Rats/Sherman-Wistar
Sex:	Males and females
# Animals:	5/sex

Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Exposure time:	One hour
Value:	> 11.7 mg/L
Method:	Other (1980). [Comparable to OECD Test Guideline 403] *Description of test procedure*: The animals were exposed to the test material inside a 260-L Plexiglas exposure chamber for one hour. The material was administered as an aerosol, which was generated by a six-jet Collision nebulizer (BGI Incorporated, Waltham, MA). The air was passed through a desiccant prior to being passed through the test material. The rate of flow through the chamber was 20 L/min at a temperature of 70°F. The average concentration of the aerosol over the one-hour exposure period was calculated to be 11.7 mg/L, by differential weighing of the flask from which the aerosol was generated. The particle size (mass median diameter) of the aerosol of the test material was determined to assure that the animals received a respirable dose and was determined using an Andersen Sampler cascade impactor. The sampler was run for 5 minutes midway through the exposure. During sampling, air from the breathing zone of the animals was drawn through the cascade impactor at the rate of 1 ft^3/min. The amount of aerosol impacting on each plate of the Andersen Sampler was determined by differential weighing. From these values the mass median diameter of the aerosol was calculated to be 0.70 microns and the concentration was calculated to be 0.24 mg/L. Following one hour of inhalation exposure, the animals were returned to their cages and observed daily for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Diisodecyl phenyl phosphite (CAS# 25550-98-5, Lot #PDDP-002-03240A from Borg Warner Company, Parkersburg, WV) Commercial, purity: Not stated (Phosphorus content = 7.09%)
Remarks:	No adverse effects were observed during the one-hour exposure period. No untoward signs and symptoms were observed during the 21-day post-exposure observation period. No animals died during the experiment and gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions.

13.3 ACUTE DERMAL TOXICITY

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rabbits/New Zealand White
Sex:	Males and females
# Animals:	3/sex

Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Value:	> 2 g/kg
Method:	Other (1980). The method employed in the testing, evaluation, and the scoring of the results was similar to the methods described in Section 1500.40 of the U.S. Federal Hazardous Substances Act Regulations, 16 CFF, pg. 123. [Comparable to OECD Test Guideline 402] *Description of test procedure*: Albino rabbits weighing between 2.0 and 3.0 kg each were employed in this study. All animals had their backs clipped free of hair 24 hours prior to testing and had their backs abraded prior to dosing. The sample was applied as supplied to the back of each animal at a dose of 5.0 g/kg body weight. These treated areas were covered with large gauze patches and an impervious material was wrapped around the trunk of each animal. The dressings were removed after 24

	hours and any excess material was removed. The animals were observed for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Diisodecyl phenyl phosphite (CAS# 25550-98-5, Lot #PDDP-002-03240A from Borg Warner Company, Parkersburg, WV) Commercial, purity: Not stated (Phosphorus content = 7.09%)
Remarks:	No remarkable findings were observed, with the exception of significant skin irritation lasting over several days. No animals died during the experiment and gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions. Comparable to OECD 402, except this limit test used 3 animals/sex rather than 5/sex as recommended by the guideline.

14.0 GENETIC TOXICITY *IN VITRO* OR *IN VIVO* (CHROMOSOMAL ABERRATIONS)

Type:	Micronucleus test
Species/strain:	Mouse/CD-1
Sex:	Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration:	Oral, gavage
Exposure period:	Two single doses administered over 24 hours
Doses:	0, 2500, 5000, and 10000 mg/kg (total dose)
Results:	*Effect on mitotic index or PCE/NCE ratio*: There was no statistically significantly difference between any of the test article treatments and the negative control. *Genotoxic effects*: Negative
Method (Year):	Other (1981). The protocol used is comparable to OECD Test Guideline 474. <u>*Description of test procedure*</u>: All animals weighted between 18 and 21 grams and were group-housed in plastic caging maintained in a controlled environment (temperature 22°C, 30 air changes/hour, 12-hour light/dark cycle, and access to food and water *ad libitum*). The animals were fasted overnight prior to dosing. A preliminary range-finding toxicity study was performed prior to the conduct of the definitive assay to determine the maximum tolerated dose (MTD) of the test article. The MTD was designed to produce one or two deaths over the treatment period. From the results of the preliminary test, doses of 0, 2500, 5000, and 10000 mg/kg were used in the main study. The test article was administered (diluted in corn oil) via oral gavage to groups of mice (5/sex), at a volume of 0.1 mL per 10 grams of body weight. The concurrent positive control group (mitomycin C) was administered by intraperitoneal injection at a concentration of 0.4 mg/mL. Following the last dose, the animals were observed for six hours, sacrificed, and both femurs removed from each

animal. A direct bone marrow smear from each femur was placed onto a slide and prepared for microscopic analysis to determine the incidence of micronucleated cells per 1000 polychromatic erythrocytes per animal and the ratio of normochromatic to polychromatic erythrocytes (PCE/NCE ratio).

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diisodecyl phenyl phosphite (CAS# 25550-98-5, Lot #PDDP-002-03240A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: Not stated (Phosphorus content = 7.09%)

Remarks: After administration of PDDP at all doses, signs of toxicity (hypopnea and lethargy) were observed 30 minutes after dosing. The symptoms decreased over the next few hours and were not observed 5 hours after each dose. At the top dose of 10000 mg/kg, there were 4 (2 males and 2 females) deaths. The animals were found dead between 2 and 5 hours after the second dose. Macroscopic examination at post mortem did not reveal abnormalities in any animal. After administration of mitomycin C, no toxic reactions or mortality were observed.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal and the PCE/NCE ratios for all test groups and both controls are presented below:

Test Group	# Micronucleated Cells per 1000 PCEs/animal mean (range)	PCE/NCE Ratio mean (range)
Negative Control	0.1 (0–1)	1.86 (1.01–4.96)
2500 g/kg PDDP	0.1 (0–1)	-*
5000 g/kg PDDP	0.3 (0–1)	-*
10000 g/kg PDDP	0.0 (0–0)	1.60 (1.23–1.81)
Mitomycin C	27.7 (7-67)	7.52 (3.24-16.37)
Historical Control	*0.79 (0.1-1.8)*	*0 - 5*

After administration of PDDP at all dosages, the group mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal was comparable to the concurrent control value and within the laboratory standard range for negative controls obtained in 18 previous experiments. The PCE/NCE ratio for the test article 10000 mg/kg was comparable to that of the negative corn oil control group.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal for the concurrent positive control group (mitomycin C) was significantly higher than the negative control group (27.7 versus 0.1, respectively). Also, the PCE/NCE for mitomycin C was significantly higher than the negative control group (7.52, range 3.24-16.37). Based on the conditions of this study, the test article, PDDP, was considered to be negative for mutagenic potential and bone marrow toxicity when administered orally.

**Criteria for evaluating results*: A material was considered to show evidence of mutagenic activity if it produced a statistically significant increase ($p>0.05$ using Wilcoxon's 'sum or ranks test') in micronucleated

cells compared to the concurrent negative control group values. If the erythrocyte ratios at the top dose were not significantly different from the concurrent negative control values, then the ratios of the two lower doses were not scored.

Reference: Richold et al. (1981). Unpublished report TCO 17C/81309 entitled "Micronucleus test on phenyldiisodecyl phosphite (PDDP)", dated June 26, 1981 for Tenneco Chemicals Inc., Saddle Brook, NJ from Huntingdon Research Centre, Cambridgeshire, England

Reliability: (Klimisch Code 1) Valid without restrictions.

15.0 GENETIC TOXICITY *IN VITRO*

15.1 BACTERIAL TEST

15.1.1

Type: Bacterial reverse mutation assay (Ames test)

System of testing: *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA 1538

Concentration: 0, 50, 100, 500, 1000, 5000 µg/plate

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 5000 µg/plate
Without metabolic activation: > 5000 µg/plate

Precipitation conc.: 1000 and 5000 µg/plate

Genotoxic effects:

	+	?	-
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

Method (Year): Based on Ames et al. (1975) *Mut. Res*., 31:347. The protocol is comparable to OECD Test Guideline 471

<u>*Description of test procedure*</u>: The test substance was dissolved in ethanol at 50 mg/mL and lower concentrations (0.5 - 10 mg/mL) were prepared by subsequent serial dilution with ethanol. One-tenth mL aliquots of these solutions were used to assay the test substance at 50 – 5000 µg/plate. Concurrent positive controls requiring metabolic activation (TA-1535, cyclophosphamide at 200 µg/plate; TA-1537, TA-1538, TA-98, and TA-100, benzo[a]pyrene at 5 µg/plate) and positive controls not requiring metabolic activation (TA-1535 and TA-100, 5 µg/plate sodium azide; TA-1537, 50 µg/plate 9-aminoacridine; TA-1538 and TA-98, 10 µg/plate 2-nitrofluorene) were run for each strain. All controls and test plates were incubated at 37^{o}C for 48 –hours, examined for the appearance of a normal background lawn, and macroscopic colonies were enumerated.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diisodecyl phenyl phosphite (CAS# 25550-98-5, Lot #PDDP-002-03240A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: Not stated (Phosphorus content = 7.09%)

Remarks: The number of revertants produced by treatment of the bacteria with the test at all concentrations and in all tester strains was less than or approximately equal to the number of revertants in the vehicle-treated

negative control groups, with and without metabolic activation. The mitotic index ranged from 0.7 to 1.5. The positive control groups were all mutagenic in their appropriate tester strains (mitotic index ranged from 4.4 to 11.3 with metabolic activation and 14.0 to 90.1 without metabolic activation), indicating that the metabolic activation system was working properly and all strains were capable of mutation. The test material PDDP was therefore concluded to not be mutagenic in this assay.

Criteria for evaluating results: The assay was scored as the ratio of the number of macroscopic colonies on the test plate over the number of macroscopic colonies on the control plate (mutation index). The test compound was considered to have a positive response if the mutagenic index was greater than 2.0 and the mutagenicity exhibited a dose-response relationship.

Plates/test: Samples were run in duplicate, with and without metabolic activation.

Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.

Media: Aqueous agar solution

Reference: Van Goethem, D. 1980. Unpublished report no 4822-E entitled "Evaluation of phenyldiisodecyl phosphite in the *Salmonella*/microsome (Ames) assay" dated September 30, 1980, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.1.2

Type: DNA repair-suspension assay

System of testing: *Escherichia coli* tester strains W3110 (pol A^+) and p3478 (pol A^-)

Concentration: 0, 0.1, 1, 5, 10, and 50 ug/mL

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 50 µg/mL
Without metabolic activation: > 50 µg/mL

Precipitation conc.: 50 µg/mL

Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative

Method (Year): Based on Slater et al. (1971) *Cancer Res*. 31:970-973.

<u>*Description of test procedure*</u>: The test substance was dissolved in ethanol at 5 mg/L. All doses were prepared by subsequent serial dilution with ethanol. Aliquots (0.1 mL) of these solutions were used to assay the test material at concentrations of 0.1 to 50 µg/mL of bacterial suspension. Plates were incubated for 18 hours at 37° C and the number of viable cells was recorded. The concurrent positive control for the metabolic activation group was 2-aminofluorene (200 µg/mL) and N-methyl-N'-nitrosoguanidine (2 µg/mL) served as the positive control for the group without metabolic activation.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diisodecyl phenyl phosphite (CAS# 25550-98-5, Lot #PDDP-002-03240A from Borg Warner Company, Parkersburg, WV)

Commercial, purity: Not stated (Phosphorus content = 7.09%)

Remarks: The survival indices at all doses for the test material were greater than 0.80 (0.83 to 0.98 without metabolic activation; 1.00 to 1.24 with metabolic activation). The survival indices for the positive controls were 0.76 and 0.36 for the groups with and without metabolic activation, respectively. The test material PDDP was therefore concluded to not cause preferential killing of the repair-deficient strain in this assay.
Criteria for evaluating results: The suspension test is scored as the ratio of the number of pol A^- survivors over the number of pol A^+ survivors (Survival Index). The test material is considered positive if the Survival Index is less than 0.8 and the differential toxicity exhibits a dose-response relationship.
Plates/test: Samples were run in duplicate, with and without metabolic activation
Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.
Media: Aqueous agar solution

Reference: Van Goethem, D. 1981. Unpublished report no. 4822-E entitled "Evaluation of phenyldiisodecyl phosphite in the E. coli DNA repair suspension assay" dated January 19, 1981, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.2 NON-BACTERIAL *IN VITRO* TEST (MAMMALIAN CELLS)

No studies were found.

16.0 REPEATED DOSE TOXICITY

No studies were found.

17.0 REPRODUCTIVE TOXICITY

No studies were found.

18.0 DEVELOPMENTAL TOXICITY/TERATOGENICITY

No studies were found.

U.S. HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

ROBUST SUMMARY

Phosphorous acid, isodecyl diphenyl ester (CAS# 26544-23-0)

Prepared by:

General Electric Company
on behalf of the
Phosphite Producers HPV Consortium

and

Phosphite Manufacturers Consortium

Washington, D.C., USA

September 10, 2001

Prepared for:

U.S. Environmental Protection Agency

Washington, D.C., USA

Table of Contents

PHOSPHOROUS ACID, ISODECYL DIPHENYL ESTER (CAS# 26544-23-0)

PHYSICAL AND CHEMICAL DATA

1.0 MELTING POINT

No studies were found.

2.0 BOILING POINT

No studies were found.

3.0 VAPOR PRESSURE

No studies were found.

4.0 PARTITION COEFFICIENT ($log_{10}P_{ow}$)

No studies were found.

5.0 WATER SOLUBILITY

5.1. Solubility

No studies were found.

5.2 pH Value, pKa Value

No studies were found.

ENVIRONMENTAL FATE AND PATHWAYS

6.0 PHOTODEGRADATION

No studies were found.

7.0 STABILITY IN WATER

No studies were found.

8.0 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS, INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

8.1. TRANSPORT

No studies were found.

8.2 THEORETICAL DISTRIBUTION (FUGACITY CALCULATION)

No studies were found.

9.0 BIODEGRADATION

No studies were found.

ECOTOXICOLOGICAL DATA

10.0 ACUTE/PROLONGED TOXICITY TO FISH

Type of Test:	Static [X] Semi-static [ ] Flow-through [ ] Other [ ] Open-system [ ] Closed-system [ ]
Species/Source:	Zebra Fish (*Brachydanio rerio*)
Exposure Period:	96 Hours
Results:	LC_{50} (96h) = > 16 mg/L (95% Confidence Limit, None) LC_{100} (96h) = > 16 mg/L LC_0 (96h) = 16 mg/L NOEC = 16 mg/L LOEC = > 16 mg/L
Analytical Monitoring:	Yes [X] No [X] ? [ ]
Method (Year):	84/449/EEC C.1 Acute toxicity for fish [Comparable to OECD 203] *Description of test procedure*: The test substance stock solution was prepared by dissolving 6.0 g into water and made up to 2000 mL. The nominal concentrations were 10, 18, 32, 58, and 100 mg/L. No carrier solvent was used. Analytical confirmation (HPLC) of test substance concentration was performed at 0 and 96-hours. Duplicate test article groups were used and compared to that of a concurrent blank (water) control group. Ten fish (supplied by West Aquarium, Lauterberg, Switzerland) per test group per tank were used. The mean fish length was 23 mm (21-26 mm) and the mean weight was 0.11 g (0.10-0.14g). The loading of fish in the tank was 0.08 g fish/L water. Fish were acclimatised for 12 days prior to the experiment and not fed for 24 hours prior to or during exposure. Each 20-L tank was filled with 15 L of dechlorinated tap water (carbon filter). The water hardness was 156 mg CaCO3/L, the temperature was maintained at 23 +/- 1^{o}C, no aeration was used, and fluorescent lighting was provided 16-hours daily. Calculated amounts of the stock solution to produce the desired test concentrations were added to

the water and homogeneously distributed. The fish were transferred into the tank for a total duration of 96-hours. Signs and symptoms of toxicity

(swimming behavior, loss of equilibrium, respiratory function, exophthalmia, and pigmentation) and mortality were recorded at 24, 48, 72, and 96-hours.

GLP: Yes [X] No [ ] ? [ ]

Test Substance: Irgastab CH 301 (CAS# 26544-23-0)
Commercial, purity: Not stated; Commercial batch no. 09520460 (Test article identification code: TK 11206) from Ciba-Geigy, Ltd, Basel, Switzerland

Remarks: The actual measured concentrations at 96-hours for the blank (water control, 10, 18, 32, 58, and 100 mg/L groups were <0.02 (detection limit), 2.0, 1.1, 0.7, 4.1, and 15.7 mg/L, respectively. All measures of toxicity were based on the actual measured concentrations at 96-hours. No fish died during the experiment and there were no effects on signs and symptoms of toxicity in any group. The oxygen content ranged from 101-105% at 0 hours, 100-105% at 24 hours, 89-92% at 48 hours, 83-96% at 72 hours, and 85-95% at 96 hours. The pH ranged from 7.9 to 8.2 and the water temperature was 23°C throughout the experiment.

Reference: Grade, R. 1993. Unpublished report no. 928299 entitled "Report on the acute toxicity test of Irgastab CH301 to Zebra-Fish (*Brachydanio rerio*)", dated June 10, 1993 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: (Klimisch Code 1) Valid without restrictions.

11.0 TOXICITY TO AQUATIC PLANTS (e.g. Algae)

Species: Green algae (*Scenedesmus subspicatus*)

End-point: Biomass [ ]; Growth rate [X]; Other [ ]

Exposure period: 72 Hours

Results: Growth: EC_{50} (72 h) = 1.6 mg/L (95% CI, None)
NOEC = < 0.02 mg/L

Analytical monitoring: Yes [X] No [ ] ? [ ]

Method (Year): open-system [ ]; closed-system [X]
87/302/EEC, Algal inhibition test [Comparable to OECD 201]
Description of test procedure: Green algae (obtained from Pflanzenphysiologisches Institut University, Gottingen, Germany) with an initial cell density of 10100 cells/mL were used in this experiment. The test vessels, 100-mL Erlenmeyer flasks stoppered with aluminum caps, were filled with 50 mL of test solution per flask. The water composition was reported to be according to the guideline, the temperature was maintained to 23 +/- 1°C, and continuous illumination of white fluorescent light (approx. 8000 lux) was used. The stock solution was made up of 20.3 mg of test substance mixed into 1000 mL of water. Calculated amounts of the stock solution to produce the desired test concentrations were added to the water and were homogeneously distributed. Nominal target concentrations of 0.123, 0.37, 1.1, 33, and 10 mg of test substance/L were used and each test concentration was tested in 3 replicates. The blank control (water) was tested in 6 replicates. The algae were transferred into the flasks for a total duration of 72 hours. Samples of each test concentration were drawn immediately before

exposure and at the end of the experiment and kept at 18-22 °C until analysed. Cell densities were measured at 24, 48, and 72 hours on a "TOA" cell counter. The EC-50 values were calculated according to the method of Berkson. (1953) *JASA* 48:569-599.

GLP: Yes [X] No [ ] ? [ ]

Test Substance: Irgastab CH 301 (CAS# 26544-23-0)
Commercial, purity: Not stated; Commercial batch no. 09520460 (Test article identification code: TK 11206) from Ciba-Geigy, Ltd, Basel, Switzerland

Remarks: The measured test substance concentrations were determined by HPLC to be <0.02, 0.1, 0.4, 1.1, 3.7, and 11.9 mg/L at 0 hours and <0.02, <0.02, <0.02, 0.07, 1.0, and 4.9 mg/L at 72 hours for the blank and the target concentrations of 0.123, 0.37, 1.1, 3.3, and 10 mg/L, respectively. The EC50 and NOEC values reported above were based on the measured concentration at 72-hours. The pH values of the water was 7.9 at 0 hours and 8.2 to 8.9 at 72 hours.

The mean cell densities (cells/mL x 10000) were as follows:

	24 hr	48 hr	72 hr
Blank	6.6	35.3	140.2
<0.02 mg/L	6.4	42.6	147.7
<0.02 mg/L	5.2	35.6	177.3
0.01 mg/L	3.5	21.0	137.3
1.0 mg/L	3.5	19.1	111.5
4.9 mg/L	1.8	8.8	42.0

The mean inhibition levels for the blank control and the <0.02, <0.02, 0.07, 1.0, and 4.9 mg/L test substance groups were 0.0, 0.0, 0.0, 17.2, 30.7, and 73.4 69.6%, respectively.

Reference: Grade, R. 1993. Unpublished report no. 928300 entitled "Report on the growth inhibition test of Irgastab CH300 to Green Algae (*Scenedesmus subspicatus*)", dated June 29, 1993 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: (Klimisch Code 1) Valid without restrictions.

12.0 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

12.1 Daphnia

Type of test: static [X]; semi-static [ ]; flow-through [ ]; other [ ]; open-system [ ]; closed-system [ ]

Species: *Daphnia magna* (Straus 1820)

Exposure period: 48 hours

Results: EC_{50} (48h) = > 1-5 mg/L (95% Confidence Limit; none)

Analytical monitoring: Yes [X] No [ ] ? [ ]

Method: 84/449/EEC C.2, Acute toxicity for *Daphnia* [Comparable to OECD 202]
Description of test procedure: Cultures of *Daphnia* (source: Ciba-Giegy ecotoxicology testing facility) were maintained in glass vessels containing

approximately 2.5 L of reconstituted water (total hardness: 294 mg/$CaCO_3$/L) at 21 +/- 1°C and fluorescent lighting was used 16 hours/day. The water was aerated with clean air for at least 24 hours prior to use and was partially renewed three times per week. At each renewal the *Daphnia* were fed with a suspension of green algae supplemented by a suspension of TETRAMIN-extract. The experimental test vessels consisted of beakers covered with watch glasses and filled with 100 mL of solution. The test substance stock solution was test substance (20.4 mg) mixed with water and made up to 1000 mL. No vehicle was used. Calculated amounts of the stock solution to produce the desired test concentrations were added to the water and were homogeneously distributed. The nominal test concentrations were 0 (blank control), 0.058, 0.1, 0.18, 0.32, 0.58, 1.0, 1.8, and 3.2 mg of test substance/L. Analytical determination (limit of detection = <0.02 mg/L) of test substance concentration was performed at 0 and 48-hours. One day prior to exposure, *Daphnia* older than 24 hours were separated from the young by sieving all individuals using an 800 µm sieve. Immediately prior to exposure, this sieving process was repeated and the young (6-24 hours of age) were retained for the test. The *Daphnia* were not fed during the test. There were a total number of 20 *Daphnia* per treatment group and control with 4 replicates of 5 *Daphnia* each. Immobilization was recorded after 24 and 48 hours of exposure. The EC-50 values were calculated according to method described by Berkson (1953; *JASA* 48:569-599), and the EC-values were graphically determined on gausso-logarithmic probability paper.

GLP: Yes [X] No [ ] ? [ ]

Test Substance: Irgastab CH 301 (CAS# 26544-23-0)
Commercial, purity: Not stated; Commercial batch no. 09520460 (Test article identification code: TK 11206) from Ciba-Geigy, Ltd, Basel, Switzerland

Remarks: The measured test substance concentrations were determined by HPLC to be <0.02, <0.02, 0.04, 0.09, 0.16, 0.47, 0.90, 1.90, and 3.30 mg/L at 0 hours for the blank and the target concentrations of 0.058, 0.1, 0.18, 0.32, 0.58, 1.0, 1.8, and 3.2 mg/L, respectively. At 48 hours, the measured concentrations were <0.02, 0.1, 0.02, 0.02, 0.09, 0.10, 0.32, 1.20, and 1.40 mg/L for the blank and the target concentrations of 0.058, 0.1, 0.18, 0.32, 0.58, 1.0, 1.8, and 3.2 mg/L, respectively. The pH values of the water ranged from 7.8 to 7.9 at both 0 and 48 hours.

The following are the percent of the immobilized *Daphnia* (n = 20 per test concentration) after 24 and 48 hours for each test group:

	24 Hours	48 Hours
Test Concentration	Total No. (%)	Total No. (%)
Blank (<0.02 mg/L)	(0)	0 (0)
0.1* mg/L	3 (15)	8 (40)
<0.02 mg/L	1 (5)	4 (20)
0.02 mg/L	4 (20)	10 (50)
0.09 mg/L	0 (0)	1 (5)
0.10 mg/L	0 (0)	3 (15)
0.32 mg/L	4 (20)	7 (35)

1.20 mg/L	2 (10)	9 (45)
1.40 mg/L	2 (10)	13 (65)

* This value was treated as an outlier

Reference: Grade, R. 1993. Unpublished report no. 928301 entitled "Report on the acute toxicity test of Irgastab CH301 on Daphnia (*Daphnia magna*, Straus 1820)", dated August 11, 1993 for Ciba-Giegy Ltd., Basel, Switzerland from Ciba-Giegy Ltd., Basel, Switzerland.

Reliability: (Klimisch Code 1) Valid without restrictions.

12.2 Other aquatic organisms

No studies were found.

TOXICITY

13.0 ACUTE TOXICITY

13.1 ACUTE ORAL TOXICITY

Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ];
Other [ ]

Species/strain: Rats/Sherman-Wistar

Sex: Males and females

Animals: 5/sex/group

Vehicle: None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).

Value: Males: 3.99 g/kg (95% Confidence Limit: 3.64 – 5.27 g/kg)
Females: 4.06 g/kg (95% Confidence Limit; 3.38 – 4.95 g/kg)

Method: Other (1981). The method employed in the testing, evaluation and the scoring of the results was adopted from the U.S. Federal Hazardous Substances Act Regulations study guidelines, 16 CFR, section 1500.3. [Comparable to OECD Test Guideline 401]
Description of test procedure: Albino rats weighing between 200 and 300 grams were dosed in an initial limit test via oral gavage with 5 g/kg body weight. For the definitive LD50 study, males received a dose of 1.58, 2.0, 2.51, 3.16, 3.55, 3.98, or 5.01 g/kg and females were administered 1.58, 2.00, 2.51, 3.16, 3.98, 5.01, or 6.31 g/kg. Animals were fasted overnight prior to dosing, but were not deprived of water. Following administration the animals were allowed food and water ad libitum for a 21-day observation period during which time the rats were observed daily for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3. The LD50 was calculated using the method described by Finney, D.J. 1971. 'Statistical Methods in Biological Assay, 2nd Edition, London Griffen Press.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diphenylisodecyl phosphite (CAS# 26544-23-0, Lot #DPDP-001-03240A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: Not stated (Phosphorus content = 8.05%)

Remarks: In the initial limit dose experiment with 5 g/kg, after 1 hour the animals (number not specified) appeared slightly lethargic and ruffled. After 2-3, the 9 out of 10 animals were comatose and died within 18 hours. The sole surviving animal appeared normal throughout the study. Gross pathological examination revealed no remarkable findings. Because the LD50 was < 5 g/kg, a definitive LD50 study was performed. The number animals that died are presented below:

Mortality Table

Males				Females			
	Study Days				Study Days		
Dose	1	2	3-21	Dose	1	2	3-21
1.58 g/kg	0	0	0	1.58 g/kg	0	0	0
2.00	0	0	0	2.00	0	0	0
2.51	0	0	0	2.51	0	0	0
3.16	0	0	0	3.16	1	0	0
3.55	1	0	0	3.98	1	1	0
3.98	1	1	0	5.01	4	0	0
5.01	5	-	-	6.31	5	-	-

At the highest dose levels in males (5.01 g/kg) and females (5.01 and 6.31 g/kg), signs of toxicity (lethargy, ruffled appearance, comatose) appeared within 1-3 hours and animals died within 1-18 hours. The sole surviving female in the 5.01 g/kg group appeared normal by the end of the observation 21-day observation period. At 3.55 and 3.98 g/kg (males) and 3.16 and 3.98 g/kg (females), signs of toxicity (lethargy and ruffled appearance) appeared within 3-4 hours and animals that did not die appeared normal within 48 hours. Those that died in these groups generally appeared severely lethargic and/or slightly comatose within 8 hours and died within 18 hours. At 2.00 and 2.51 g/kg in males and females, only slight lethargy was observed between 18-24 hours and all animals of these groups appeared normal by 48-hours. There were no signs and symptoms of toxicity in either sex at 1.58 g/kg. Gross pathological examination revealed nothing remarkable.

Reference: Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA

Reliability: (Klimisch Code 1) Valid without restrictions.

13.2 ACUTE INHALATION TOXICITY

(a)

Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [X]; LCL_0 [ ]; Other [ ]

Species/strain: Rats/Sherman-Wistar

Sex: Males and females

# Animals:	5/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Exposure time:	One hour
Value:	> 8.4 mg/L (maximum attainable concentration)
Method:	Other (1980). [Comparable to OECD Test Guideline 403] *Description of test procedure*: The animals were exposed to the test material inside a 260-L Plexiglas exposure chamber for one hour. The material was administered as an aerosol, which was generated by a six-jet Collision nebulizer (BGI Incorporated, Waltham, MA). The air was passed through a desiccant prior to being passed through the test material. The rate of flow through the chamber was 20 L/min at a temperature of 72^{o}F. The average concentration of the aerosol over the one-hour exposure period was calculated to be 8.4 mg/L, by differential weighing of the flask from which the aerosol was generated. The particle size (mass median diameter) of the aerosol of the test material was determined to assure that the animals received a respirable dose and was determined using an Andersen Sampler cascade impactor. The sampler was run for 5 minutes midway through the exposure. During sampling, air from the breathing zone of the animals was drawn through the cascade impactor at the rate of 1 ft^{3}/min. The amount of aerosol impacting on each plate of the Andersen Sampler was determined by differential weighing. From these values the mass median diameter of the aerosol was calculated to be 0.80 microns and the concentration was calculated to be 0.16 mg/L. Following one hour of inhalation exposure the animals were returned to their cages and observed daily for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Diphenylisodecyl phosphite (CAS# 26544-23-0, Lot #DPDP-001-03240A from Borg Warner Company, Parkersburg, WV) Commercial, purity: Not stated (Phosphorus content = 8.05%)
Remarks:	No adverse effects were observed during the one-hour exposure period. No untoward signs and symptoms were observed during the 21-day post exposure observation period. No animals died during the experiment and gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions. Acceptable, well documented study report that meets basic scientific principles.

13.3 ACUTE DERMAL TOXICITY

(a)

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rabbits/New Zealand White

Sex:	Males and females
# Animals:	3/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Value:	> 5 g/kg
Method:	Other (1980). The method employed in the testing, evaluation and the scoring of the results was similar to the methods described in Section 1500.40 of the U.S. Federal Hazardous Substances Act Regulations, 16 CFF, pg. 123. [Comparable to OECD Test Guideline 402] *Description of test procedure*: Albino rabbits weighing between 2.0 and 3.0 kg each were used in this study. All animals had their backs clipped free of hair 24 hours prior to testing and had their backs abraded prior to dosing. The sample was applied as supplied to the back of each animal at a dose of 5.0 g/kg body weight. These treated areas were covered with large gauze patches and an impervious material was wrapped around the trunk of each animal. The dressings were removed after 24 hours and any excess material was removed. The animals were observed for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.
GLP:	Yes [X] No [ ] ? [ ]
Test substance:	Diphenylisodecyl phosphite (CAS# 26544-23-0, Lot #DPDP-001-03240A from Borg Warner Company, Parkersburg, WV) Commercial, purity: Not stated (Phosphorus content = 8.05%)
Remarks:	No remarkable findings were observed, with the exception of significant skin irritation lasting over several days. No animals died during the experiment and gross pathological examination revealed no remarkable findings.
Reference:	Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA
Reliability:	(Klimisch Code 1) Valid without restrictions. Comparable to OECD 402 except this limit test used 3 animals/sex rather than 5/sex as recommended by the guideline.

14.0 GENETIC TOXICITY *IN VITRO* OR *IN VIVO* (CHROMOSOMAL ABERRATIONS)

(a)

Type:	Micronucleus test
Species/strain:	Mouse/CD-1
Sex:	Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
Route of Administration:	Oral, gavage
Exposure period:	Two single doses administered over 24 hours
Doses:	0, 2250, 4500, and 9000 mg/kg (total dose)
Results:	*Effect on mitotic index or PCE/NCE ratio*: There was no statistically significantly difference between any of the test article treatments and the negative control. *Genotoxic effects*: Negative

Method (Year): Other (1981). The protocol used is comparable to OECD Test Guideline 474

Description of test procedure: All animals weighted between 18 and 21 grams and were group-housed in plastic caging maintained in a controlled environment (temperature 22°C, 30 air changes/hour, 12-hour light/dark cycle, and access to food and water ad libitum). The animals were fasted overnight prior to dosing. A preliminary range-finding toxicity study was performed prior to the conduct of the definitive assay to determine the maximum tolerated dose (MTD) of the test article. The MTD was designed to produce one or two deaths over the treatment period. From the results of the preliminary test, doses of 0, 2250, 4500, and 9000 mg/kg were used in the main study. The test article was administered (diluted in corn oil) via oral gavage to groups of mice (5/sex), at a volume of 0.1 mL per 10 grams of body weight. The concurrent positive control group (mitomycin C) was administered by intraperitoneal injection at a concentration of 0.4 mg/mL. Following the last dose, the animals were observed for six hours, sacrificed, and both femurs removed from each animal. A direct bone marrow smear from each femur was placed onto a slide and prepared for microscopic analysis to determine the incidence of micronucleated cells per 1000 polychromatic erythrocytes per animal and the ratio of normochromatic to polychromatic erythrocytes (PCE/NCE ratio).

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diphenylisodecyl phosphite (CAS# 26544-23-0, Lot #DPDP-001-03240A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: Not stated (Phosphorus content = 8.05%)

Remarks: After administration of DPDP at 9000 mg/kg, signs of toxicity (hypopnea and lethargy) were observed 30 minutes after dosing in both sexes. The symptoms decreased over the next few hours and were not observed 3 hours after administration. A single female died within 7 hours after this highest dose. Macroscopic examination at post mortem did not reveal abnormalities in any animal. No toxic reactions were observed in the corn oil negative control group or the 2250 and 4500 mg/kg group. After administration of mitomycin C, no toxic reactions or mortality were observed.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal and the PCE/NCE ratios for all test groups and both controls are presented below:

Test Group	# Micronucleated Cells per 1000 PCEs/animal mean (range)	PCE/NCE Ratio mean (range)
Negative Control	0.4 (0–2)	2.69 (1.19–5.29)
2250 g / kg DPDP	0.4 (0–1)	-*
4500 g/kg DPDP	1.1 (0-3)	-*
9000 g/kg DPDP	0.8 (0–2)	2.32 (1.36–3.27)
Mitomycin C	32.2 (9-96)	9.09 (14.73)
Historical Control	*0.79 (0.1-1.8)*	*0 - 5*

After administration of DPDP at all dosages, the group mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal was comparable to the concurrent control value and within the laboratory standard range for negative controls obtained in 18 previous experiments. The PCE/NCE ratio for the test article at 9000 mg/kg was comparable to that of the negative corn oil control group.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal for the concurrent positive control group (mitomycin C) was significantly higher than the negative control group. Also, the PCE / NCE for mitomycin C was significantly higher than the negative control group.

Based on the conditions of this study, the test article, DPDP, was considered to be negative for mutagenic potential and bone marrow toxicity when administered orally.

**Criteria for evaluating results*: A material was considered to show evidence of mutagenic activity if it produced a statistically significant increase ($p>0.05$ using Wilcoxon's 'sum or ranks test') in micronucleated cells compared to the concurrent negative control group values. If the erythrocyte ratios at the top dose were not significantly different from the concurrent negative control values then the ratios of the two lower doses were not scored.

Reference: Richold et al. (1981). Unpublished report TCO 17D/81310 entitled "Micronucleus test on diphenylisodecyl phosphite (DPDP)", dated June 26, 1981 for Tenneco Chemicals Inc., Saddle Brook, NJ from Huntingdon Research Centre, Cambridgeshire, England

Reliability: (Klimisch Code 1) Valid without restrictions.

15.0 GENETIC TOXICITY *IN VITRO*

15.1 BACTERIAL TEST

15.1.1

Type: Bacterial reverse mutation assay (Ames test)

System of testing: *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA 1538

Concentration: 0, 50, 100, 500, 1000, 5000 µg/plate

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 5000 µg/plate
Without metabolic activation: > 5000 µg/plate

Precipitation conc.: 1000 and 5000 µg/plate

Genotoxic effects:

	+	?	-
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

Method (Year): Based on Ames et al. (1975) *Mut. Res*., 31:347. The protocol is comparable to OECD Test Guideline 471
Description of test procedure: The test substance was dissolved in ethanol at 50 mg/mL and lower concentrations (0.5 - 10 mg/mL) were prepared

by subsequent serial dilution with ethanol. One-tenth mL aliquots of these solutions were used to assay the test substance at 50 – 5000 μg/plate. Concurrent positive controls requiring metabolic activation (TA-1535, cyclophosphamide at 200 μg/plate; TA-1537, TA-1538, TA-98, and TA-100, benzo[a]pyrene at 5 μg/plate) and positive controls not requiring metabolic activation (TA-1535 and TA-100, 1 μg/plate sodium azide; TA-1537, 50 μg/plate 9-aminoacridine; TA-1538 and TA-98, 10 μg/plate 2-nitrofluorene) were run for each strain. All controls and test plates were incubated at 37 ^{o}C for 48 hours, examined for the appearance of a normal background lawn, and macroscopic colonies were enumerated.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diphenylisodecyl phosphite (CAS# 26544-23-0, Lot #DPDP-001-03240A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: Not stated (Phosphorus content = 8.05%)

Remarks: The number of revertants produced by treatment of the bacteria with the test at all concentrations and in all tester strains was less than or approximately equal to the number of revertants in the vehicle-treated negative control groups, with and without metabolic activation. The mutagenic index ranged from 0.6 to 1.5, with the exception of the 10 ug/plate S-9 group with strain TA-1537 (2.4) and the 1000 ug/plate group without S-9 in strain TA-100 (6.0). Although these two values were about the value of 2.0, they did not exhibit a dose-response pattern. The positive control groups were all mutagenic in their appropriate tester strains (mitotic index ranged from 4.0 to 15.9 with metabolic activation and 8.6 to 68.0 without metabolic activation), indicating that the metabolic activation system was working properly and all strains were capable of mutation. The test material DPDP was therefore concluded to not be mutagenic in this assay.
Criteria for evaluating results: The assay was scored as the ratio of the number of macroscopic colonies on the test plate over the number of macroscopic colonies on the control plate (mutagenic index). The test compound was considered to have a positive response if the mutagenic index was greater than 2.0 and the mutagenicity exhibited a dose response relationship.
Plates/test: Samples were run in duplicate, with and without metabolic activation.
Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.
Media: Aqueous agar solution

Reference: Van Goethem, D. 1980. Unpublished report no 4822-E entitled "Evaluation of diphenylisodecyl phosphite in the *Salmonella*/microsome (Ames) assay" dated September 15, 1980, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.1.2

Type: DNA repair-suspension assay

System of testing: *Escherichia coli* tester strains W3110 (pol A^{+}) and p3478 (pol A^{-})

Concentration: 0, 0.1, 1, 5, 10, and 50 μg/mL

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 50 μg/mL
Without metabolic activation: > 50 μg/mL

Precipitation conc.: 50 μg/mL

Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative

Method (Year): Based on Slater et al. (1971) *Cancer Res*. 31:970-973.
Description of test procedure: The test substance was dissolved in ethanol at 5 mg/L. All doses were prepared by subsequent serial dilution with ethanol. Aliquots (0.1 mL) of these solutions were used to assay the test material at concentrations of 0.1 to 50 μg/mL of bacterial suspension. Plates were incubated for 18 hours at 37°C and the number of viable cells was recorded. The concurrent positive control for the metabolic activation group was 2-aminofluorene (200 μg/mL) and N-methyl-N'-nitrosoguanidine (2 μg/mL) served as the positive control for the group without metabolic activation.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Diphenylisodecyl phosphite (CAS# 26544-23-0, Lot #DPDP-001-03240A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: Not stated (Phosphorus content = 8.05%)

Remarks: The survival indices at all doses for the test material were greater than 0.80 with or without metabolic activation (0.87 to 1.35 without metabolic activation; 0.93 to 1.07 with metabolic activation). The survival indices for the positive controls were 0.76 and 0.62 for the groups with and without metabolic activation, respectively. The test material PDDP was therefore concluded to not cause preferential killing of the repair-deficient strain in this assay.
Criteria for evaluating results: The suspension test is scored as the ratio of the number of pol A^- survivors over the number of pol A^+ survivors (Survival Index). The test material is considered positive if the Survival Index is less than 0.8 and the differential toxicity exhibits a dose response relationship.
Plates/test: Samples were run in duplicate with and without metabolic activation.
Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.
Media: Aqueous agar solution

Reference: Van Goethem, D. 1981. Unpublished report no. 4822-E entitled "Evaluation of diphenylisodecyl phosphite in the E. coli DNA repair suspension assay" dated January 22, 1981, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.2 NON-BACTERIAL *IN VITRO* TEST (MAMMALIAN CELLS)

No studies were found.

16.0 REPEATED DOSE TOXICITY

No studies were found.

17.0 REPRODUCTIVE TOXICITY

No studies were found.

18.0 DEVELOPMENTAL TOXICITY/TERATOGENICITY

No studies were found.

U.S. HIGH PRODUCTION VOLUME (HPV)
CHEMICAL CHALLENGE PROGRAM

ROBUST SUMMARY

Phosphorous acid, triphenyl ester (CAS# 101-02-0)

Prepared by:

General Electric Company
on behalf of the
Phosphite Producers HPV Consortium

and

Phosphite Manufacturers Consortium

Washington, D.C., USA

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PHOSPHOROUS ACID, TRIPHENYL ESTER (CAS# 101-02-0)

PHYSICAL AND CHEMICAL DATA

1.0 MELTING POINT

No studies were found.

2.0 BOILING POINT

No studies were found.

3.0 VAPOR PRESSURE

No studies were found.

4.0 PARTITION COEFFICIENT ($log_{10}P_{ow}$)

No studies were found.

5.0 WATER SOLUBILITY

5.1 Solubility

No studies were found.

5.2 pH Value, pKa Value

No studies were found.

ENVIRONMENTAL FATE AND PATHWAYS

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No studies were found.

7.0 STABILITY IN WATER

No studies were found.

8.0 TRANSPORT AND DISTRIBUTION BETWEEN ENVIRONMENTAL COMPARTMENTS, INCLUDING ESTIMATED ENVIRONMENTAL CONCENTRATIONS AND DISTRIBUTION PATHWAYS

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No studies were found.

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No studies were found.

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No studies were found.

ECOTOXICOLOGICAL DATA

10.0 ACUTE/PROLONGED TOXICITY TO FISH

No studies were found.

11.0 TOXICITY TO AQUATIC PLANTS (e.g., Algae)

No studies were found.

12.0 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

No studies were found.

TOXICITY

13.0 ACUTE TOXICITY

13.1 ACUTE ORAL TOXICITY

Type:	LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ]; Other [ ]
Species/strain:	Rats/Sherman-Wistar
Sex:	Males and females
# Animals:	5/sex
Vehicle:	None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).
Value:	Males: 1.59 g/kg (95% Confidence Limit: 1.45 – 2.13 g/kg)

Females: 1.63 g/kg (95% Confidence Limit; 1.40 – 1.88 g/kg)

Method: Other (1981). The method employed in the testing, evaluation, and the scoring of the results was adopted from the U.S. Federal Hazardous Substances Act Regulations study guidelines, 16 CFR, section 1500.3. [Comparable to OECD Test Guideline 401]

Description of test procedure: Albino rats weighing between 200 and 300 grams were dosed in an initial limit test via oral gavage with 5 g/kg body weight. For the definitive LD50 study, males received a dose of either 1.00, 1.26, 1.41, 1.58, 2.00, 2.51, 3.16, and 3.98 g/kg and females were administered 1.00, 1.26, 1.58, 1.78, 2.00, 2.51, 3.16, and 3.98 g/kg. Animals were fasted overnight, but were not deprived of water. Following administration the animals were allowed food and water *ad libitum* for a 21-day observation period, during which time the rats were observed daily for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3. The LD50 was calculated using the method described by Finney, D.J. 1971. 'Statistical Methods in Biological Assay, 2nd Edition, London Griffen Press.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triphenyl phosphite (CAS# 101-02-0, Lot #TPPx-Z18-04080A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: ≥ 97% (Phosphorus content = 10.0 %)

Remarks: In the initial limit dose experiment with 5 g/kg, within 1 hour the animals were depressed and ruffled, after 2-3 hours the animals were comatose. All animals died within 18 hours. Gross pathological examination revealed no remarkable findings. Because the LD50 was < 5 g/kg, a definitive LD50 study was performed. The doses and number animals at each dose that died are presented below:

Mortality Table

Males				Females			
	Study Days				Study Days		
Dose	1	2	3-21	Dose	1	2	3-21
1.00 g/kg	0	0	0	1.00 g/kg	0	0	0
1.26	0	0	0	1.26	1	0	0
1.41	1	0	0	1.58	1	0	0
1.58	2	0	0	1.78	3	0	0
2.00	5	-	-	2.00	5	-	-
2.51	5	-	-	2.51	5	-	-
3.16	5	-	-	3.16	5	-	-
3.98	5	-	-	3.98	5	-	-

At the highest four doses in both males and females (2.00 to 3.98 g/kg), signs of toxicity (severe depression, ruffled appearance, drooling, ataxia) appeared within 1-2 hours, the animals became comatose within 2-3 hours, and died within 1-18 hours. At the lower doses in males (1.26 to 1.58) and females (1.26 to 1.78), signs of toxicity were not as severe (slight or moderate depression, ruffled appearance, drooling) after 1-2 hours. Those that died became severely lethargic and comatose after 3-4 hours and were found dead within 18 hours. Those that survived at these

doses appeared recovered and normal within 24-48 hours. At a dose of 1.00 g/kg in males and females, animals were slightly depressed and ruffled after a few hours and appeared normal by 24 hours. Gross pathological examination revealed nothing remarkable.

Reference: Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA

Reliability: (Klimisch Code 1) Valid without restrictions.

13.2 ACUTE INHALATION TOXICITY

Type: LC_0 [ ]; LC_{100} [ ]; LC_{50} [X]; LCL_0 [ ]; Other [ ]

Species/strain: Rats/Sherman-Wistar

Sex: Males and females

Animals: 5/sex

Vehicle: None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).

Exposure time: One hour

Value: > 6.7 mg/L (maximum attainable concentration)

Method: Other (1980). [Comparable to OECD Test Guideline 403]

Description of test procedure: The animals were exposed to the test material inside a 260-L Plexiglas exposure chamber for one hour. The material was administered as an aerosol, which was generated by a six-jet Collision nebulizer (BGI Incorporated, Waltham, MA). The air was passed through a desiccant prior to being passed through the test material. The rate of flow through the chamber was 20 L/min at a temperature of 72^o F. The average concentration of the aerosol over the one-hour exposure period was calculated to be 6.7 mg/L by differential weighing of the flask from which the aerosol was generated. The particle size (mass median diameter) of the aerosol of the test material was determined, to assure that the animals received a respirable dose, using an Andersen Sampler cascade impactor. The sampler was run for 5 minutes midway through the exposure. During sampling, air from the breathing zone of the animals was drawn through the cascade impactor at the rate of 1 ft^3/min. The amount of aerosol impacting on each plate of the Andersen Sampler was determined by differential weighing. From these values the mass median diameter of the aerosol was calculated to be 0.73 microns and the concentration was calculated to be 0.24 mg/L. Following one hour of inhalation exposure, the animals were returned to their cages and observed daily for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triphenyl phosphite (CAS# 101-02-0, Lot #TPPx-Z18-04080A from Borg Warner Company, Parkersburg, WV)

Commercial, purity: $\geq$ 97% (Phosphorus content = 10.0 %)

Remarks: No adverse effects were observed during the one-hour exposure period. No untoward signs and symptoms were observed during the 21-day post

exposure observation period. No animals died during the experiment and gross pathological examination revealed no remarkable findings.

Reference: Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA

Reliability: (Klimisch Code 1) Valid without restrictions.

13.3 ACUTE DERMAL TOXICITY

Type: LD_0 [ ]; LD_{100} [ ]; LD_{50} [X]; LDL_0 [ ];
Other [ ]

Species/strain: Rabbits/New Zealand White

Sex: Males and females

Animals: 3/sex

Vehicle: None used. The sample was dosed as supplied (described as a colorless to straw-colored liquid).

Value: > 2 g/kg but < 5 g/kg

Method: Other (1980). The method employed in the testing, evaluation, and the scoring of the results was similar to the methods described in Section 1500.40 of the U.S. Federal Hazardous Substances Act Regulations, 16 CFF, pg. 123. [Comparable to OECD Test Guideline 402]

Description of test procedure: Albino rabbits weighing between 2.0 and 3.0 kg each were used in this study. All animals had their backs clipped free of hair 24 hours prior to testing and had their backs abraded prior to dosing. The sample was applied as supplied to the back of each animal at a dose of 5.0 g/kg body weight. These treated areas were covered with large gauze patches and an impervious material was wrapped around the trunk of each animal. The dressings were removed after 24 hours and any excess material was removed. The animals were observed for a 21-day period for signs of toxicity and mortality. The animals were housed and maintained in compliance with the Animal Welfare Act (Pub. L-94-279) 9 CFR, Part 3.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triphenyl phosphite (CAS# 101-02-0, Lot #TPPx-Z18-04080A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: $\geq$ 97% (Phosphorus content = 10.0 %)

Remarks: At a dose of 5 g/kg, all three males and females died. After 5-6 hours, the animals appeared cold, and lethargic. They became semi-comatose after 18 hours and deaths occurred over approximately 2-3 days after dosing. At 2 g/kg, no animals died and there were no remarkable findings, except for substantial skin irritation lasting over several days. Gross pathological examination revealed no remarkable findings.

Reference: Gabriel, K.L. 1980. Unpublished report no. 80-2010A entitled "Summary of results of acute toxicity studies", dated September 26, 1980 for Tenneco Chemicals Inc., Saddle Brook, NJ from Biosearch Inc., Philadelphia, PA

Reliability: (Klimisch Code 1) Valid without restrictions. Comparable to OECD 402, except this limit test used 3 animals/sex rather than 5/sex as recommended by the OECD guideline.

14.0 GENETIC TOXICITY *IN VITRO* OR *IN VIVO* (CHROMOSOMAL ABERRATIONS)

Type: Micronucleus test
Species/strain: Mouse/CD-1
Sex: Female [ ]; Male [ ]; Male/Female [X]; No data [ ]
# of Animals: 5/sex
Route of Administration: Oral, gavage
Exposure period: Two single doses administered over 24 hours
Doses: 0, 1250, 2500, and 5000 mg/kg (total dose)
Results: *Effect on mitotic index or PCE/NCE ratio*: There was no statistically significantly difference between any of the test article treatments and the negative control.
Genotoxic effects: Negative
Method (Year): Other (1981). The protocol used is comparable to OECD Test Guideline 474
Description of test procedure: All animals weighted between 18 and 21 grams and were grouped housed in plastic caging maintained in a controlled environment (temperature 22^{o}C, 30 air changes/hour, 12-hour light/dark cycle, and access to food and water *ad libitum*). The animals were fasted overnight prior to dosing. A preliminary range-finding toxicity study was performed prior to the conduct of the definitive assay to determine the maximum tolerated dose (MTD) of the test article. The MTD was designed to produce one or two deaths over the treatment period. From the results of the preliminary test, doses of 0, 1250, 2500, and 5000 mg/kg were used in the main study. The test article was administered (diluted in corn oil) via oral gavage to groups of mice (5/sex), at a volume of 0.1 mL per 10 grams of body weight. The concurrent positive control group was given an intraperitoneal injection of mitomycin C at a concentration of 0.4 mg/mL. Following the last dose, the animals were observed for six hours, sacrificed, and both femurs were removed from each animal. A direct bone marrow smear from each femur was placed onto a slide and prepared for microscopic analysis to determine the incidence of micronucleated cells per 1000 polychromatic erythrocytes per animal and the ratio of normochromatic to polychromatic erythrocytes (PCE/NCE ratio).
GLP: Yes [X] No [ ] ? [ ]
Test substance: Triphenyl phosphite (CAS# 101-02-0, Lot #TPPx-Z18-04080A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: $\geq$ 97% (Phosphorus content = 10.0 %)
Remarks: After administration of TPP at 1250 and 2500, no signs of toxicity were observed in either sex. At a dose of 5000 mg/kg, five animals (3 male/2 female) died within 48 hours. Signs of toxicity at this dose included tremors observed 30 minutes after dosing in both males and females. The tremors decreased in severity over the next hour and were not evident after 2 hours. Gross necropsy revealed no remarkable findings. No toxic

reactions were observed in the corn oil negative control group or the 4450 mg/kg group in either sex. After administration of mitomycin C, no toxic reactions or mortality were observed in either sex.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal and the PCE/NCE ratios for all test groups and both controls are presented below:

	# Micronucleated Cells per 1000 PCEs/animal	PCE/NCE Ratio
Test Group	mean (range)	mean (range)
Negative Control	0.1 (0–1)	1.86 (1.01–4.96)
1250 g / kg TPP	0.2 (0–1)	-
2500 g/kg TPP	0.2 (0–1)	-
5000 g/kg TPP	0.2 (0–1)	1.38 (1.09–1.86)
Mitomycin C	27.7 (7-67)	7.52 (3.24-16.37)
Historical Control	*0.79 (0.1-1.8)*	*0 - 5*

After administration of TPP at all dosages in both sexes, the group mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal was comparable to the concurrent control value and within the laboratory standard range for negative controls obtained in 18 previous experiments. The PCE/NCE ratio for the test article at 5000 mg/kg in both sexes was comparable to that of the negative corn oil control group.

The mean number of micronucleated cells per 1000 polychromatic erythrocytes per animal for the concurrent positive control group (mitomycin C) was significantly higher than the negative control group. Also, the PCE / NCE for mitomycin C was significantly higher than the negative control group.

Based on the conditions of this study, it was concluded that the test article, TPP, was considered to be negative in both sexes for mutagenic potential and bone marrow toxicity when administered orally.

Criteria for evaluating results: A material was considered to show evidence of mutagenic activity if it produced a statistically significant increase ($p>0.05$ using Wilcoxon's 'sum or ranks test') in micronucleated cells compared to the concurrent negative control group values. If the erythrocyte ratios at the top dose were not significantly different from the concurrent negative control values, then the ratios of the two lower doses were not scored.

Reference: Richold et al. (1981). Unpublished report TCO 17B/81308 entitled "Micronucleus test on triphenyl phosphite (TPP)", dated June 26, 1981 for Tenneco Chemicals Inc., Saddle Brook, NJ from Huntingdon Research Centre, Cambridgeshire, England

Reliability: (Klimisch Code 1) Valid without restrictions.

15.0 GENETIC TOXICITY *IN VITRO*

15.1 BACTERIAL TEST

15.1.1

Type: Bacterial reverse mutation assay (Ames test)

System of testing: *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA 1538

Concentration: 0, 5, 10, 50, 100, 500 µg/plate

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 500 μg/plate
Without metabolic activation: > 500 μg/plate
Precipitation conc.: 50, 100 and 500 μg/plate
Genotoxic effects:

	+	?	-
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

Method (Year): Based on Ames et al. (1975) *Mut. Res*., 31:347. The protocol is comparable to OECD Test Guideline 471

Description of test procedure: The test substance was dissolved in ethanol at 50 mg/mL and lower concentrations (0.05, 0.1, 0.5, and 1.0 mg/mL) were prepared by subsequent serial dilution with ethanol. One-tenth mL aliquots of these solutions were used to assay the test substance at 5 – 500 μg/plate. Concurrent positive controls requiring metabolic activation (TA-1535, cyclophosphamide at 200 μg/plate; TA-1537, TA-1538, TA-98, and TA-100, benzo[a]pyrene at 5 μg/plate) and positive controls not requiring metabolic activation (TA-1535 and TA-100, 1 μg/plate sodium azide; TA-1537, 50 μg/plate 9-aminoacridine; TA-1538 and TA-98, 10 μg/plate 2-nitrofluorene) were run for each strain. All controls and test plates were incubated at 37°C for 48 –hours, examined for the appearance of a normal background lawn, and macroscopic colonies were enumerated.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triphenyl phosphite (CAS# 101-02-0, Lot #TPPx-Z18-04080A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: ≥ 97% (Phosphorus content = 10.0 %)

Remarks: The number of revertants produced by treatment of the bacteria with the test at all concentrations and in all tester strains was less than or approximately equal to the number of revertants in the vehicle-treated negative control groups, with and without metabolic activation. The mutagenic indices ranged from 0.6 to 1.2 without S-9 mix and from 0.5 to 1.3 with S-9 mix in all TPP test groups. The positive control groups were all mutagenic in their appropriate tester strains (mitotic index ranged from 6.1 to 11.4 with metabolic activation and from 5.0 to 109.8 without metabolic activation), indicating that the metabolic activation system was working properly and all strains were capable of mutation. The test material TPP was therefore concluded to not be mutagenic in this assay.

Criteria for evaluating results: The assay was scored as the ratio of the number of macroscopic colonies on the test plate over the number of macroscopic colonies on the control plate (mutagenic index). The test compound was considered to have a positive response if the mutagenic index was greater than 2.0 and the mutagenicity exhibited a dose-response relationship.

Plates/test: Samples were run in duplicate, with and without metabolic activation.

Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.

Media: Aqueous agar solution

Reference: Van Goethem, D. 1980. Unpublished report no 4822-E entitled "Evaluation of triphenyl phosphite in the *Salmonella*/microsome (Ames)

assay" dated September 15, 1980, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.1.2

Type: Bacterial reverse mutation assay (Ames test)

System of testing: *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA 1537

Concentration: 0, 100, 333, 1000, 3333, and 10000 μg/plate

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 10000 μg/plate
Without metabolic activation: > 10000 μg/plate

Precipitation conc.: ≥ 1000 μg/plate

Genotoxic effects:

	+	?	-
With metabolic activation:	[ ]	[ ]	[X]
Without metabolic activation:	[ ]	[ ]	[X]

Method (Year): Based on Haworth et al., 1983, Environ Mutagen 5(1):3-142. The protocol is comparable to OECD Test Guideline 471

Description of test procedure: A total of 255 chemicals were tested for mutagenicity at various laboratories and at different times. All testing was performed at Case Western University, EG&G Mason Research Institute (now known as BioReliance Inc.), or SRI International. For TPP, the laboratory was Case Western University. All strains of *Salmonella typhimurium* were obtained from Dr. Bruce Ames (University of California, Berkeley). Prior to their use for mutagenicity assays, all cultures were grown overnight with shaking at 37° C in Oxoid broth, and their phenotypes were analyzed. The test chemical, *Salmonella* culture, and S-9 mix or buffer were incubated at 37° C, without shaking, for 20 minutes. The agar was then added and the contents of the test tubes were mixed and poured onto the surface of petri dishes that contained Vogel-Bonner medium. The histidine-revertant colonies arising on these plates were counted using an automatic colony counter after 2 days of incubation at 37° C, or counted by hand when a precipitate formed. All test concentrations were tested in triplicate and the experiments were repeated approximately 1 week later. Concurrent solvent and positive controls were run with each trial. The solvent control for TPP was DMSO. Positive controls used without metabolic activation included sodium azide (TA1535 and TA100), 9-aminoacridine (TA97 and TA1537), and 4-nitro-*o*-phenylenediamine (TA98). The compound used with metabolic activation included 9-aminoacridine for all strains. The S-9 fractions were derived from Aroclor 1254-induced male Sprague-Dawley rat and male Syrian hamster livers.

GLP: Yes [ ] No [ ] ? [X]

Test substance: Triphenyl phosphite (CAS# 101-02-0) from Aldrich with an analyzed purity of 94.1%

Remarks: The number of his^+ revertants/plate produced by treatment of the bacteria with the test at all concentrations and in all tester strains was similar to the number of his^+ revertants/plate in the vehicle-treated negative control group, with and without metabolic activation. The positive control groups

were all mutagenic in their appropriate tester strains, indicating that the metabolic activation system was working properly and all strains were capable of mutation. The test material TPP was therefore concluded to not be mutagenic in this assay.

Criteria for evaluating results: A test material was judged to be positive for mutagenicity if it produced a reproducible, dose-related increase in histadine revertants over the corresponding solvent controls in replicate trials.

Reference: Zeiger et al., 1987. Salmonella mutagenicity tests: III. Results from the testing of 255 chemicals. *Environmental Mutagenesis*, 9(9): 1-110.

Reliability: (Klimisch Code 2) Valid without restrictions. Acceptable, well-documented publication that meets basic scientific principles.

15.1.3

Type: DNA repair-suspension assay

System of testing: *Escherichia coli* tester strains W3110 (pol A^+) and p3478 (pol A^-)

Concentration: 0, 0.1, 1, 5, 10, and 50 µg/mL

Metabolic activation: With [ ]; Without [ ]; With and Without [X];
No data [ ]

Results: Negative

Cytotoxicity conc.: With metabolic activation: > 50 µg/mL
Without metabolic activation: > 50 µg/mL

Precipitation conc.: 50 µg/mL

Genotoxic effects:
With metabolic activation: Negative
Without metabolic activation: Negative

Method (Year): Based on Slater et al. (1971) *Cancer Res*. 31:970-973.

Description of test procedure: The test substance was dissolved in ethanol at 5 mg/L. All doses were prepared by subsequent serial dilution with ethanol. Aliquots (0.1 mL) of these solutions were used to assay the test material at concentrations of 0.1 to 50 µg/mL of bacterial suspension. Plates were incubated for 18 hours at 37°C and the number of viable cells was recorded. The concurrent positive control for the metabolic activation group was 2-aminofluorene (200 µg/mL) and N-methyl-N'-nitrosoguanidine (2 µg/mL) served as the positive control for the group without metabolic activation.

GLP: Yes [X] No [ ] ? [ ]

Test substance: Triphenyl phosphite (CAS# 101-02-0, Lot #TPPx-Z18-04080A from Borg Warner Company, Parkersburg, WV)
Commercial, purity: $\geq$ 97% (Phosphorus content = 10.0 %)

Remarks: The survival indices at all doses for the test material were greater than 0.80, with or without metabolic activation (0.83 to 1.35 without metabolic activation; 0.86 to 1.14 with metabolic activation). The survival indices for the positive controls were 0.62 and 0.47 for the groups with and without metabolic activation, respectively. The test material TPP was therefore concluded to not cause preferential killing of the repair-deficient strain in this assay.

Criteria for evaluating results: The suspension test is scored as the ratio of the number of pol A^- survivors over the number of pol A^+ survivors (Survival Index). A test material is considered positive if the Survival

Index is less than 0.8 and the differential toxicity exhibits a dose response relationship.
Plates/test: Samples were run in duplicate, with and without metabolic activation.
Activation system: The S-9 fraction from rat liver was induced with Aroclor 1254 and prepared just prior to use.
Media: Aqueous agar solution

Reference: Van Goethem, D. 1980. Unpublished report no 4822-E entitled "Evaluation of triphenyl phosphite in the *Salmonella*/microsome (Ames) assay" dated September 15, 1980, for Tenneco Chemicals, Inc. Saddle Brook, NJ from Midwest Research Institute, Kansas City, MO.

Reliability: (Klimisch Code 1) Valid without restrictions.

15.2 NON-BACTERIAL *IN VITRO* TEST (MAMMALIAN CELLS)

No studies were found.

16.0 REPEATED DOSE TOXICITY

No studies were found.

17.0 REPRODUCTIVE TOXICITY

No studies were found.

18.0 DEVELOPMENTAL TOXICITY/TERATOGENICITY

No studies were found.